Summary of Research on the Association of Autism and Immunizations

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SARRC
Southwest Autism Research & Resource Center

What is Autism?

Social interaction

Communication (verbal and nonverbal)

Stereotyped behaviors, interests, and activities

ASD is a developmental disorder

- Both positive (abnormal) behaviors and negative (the absence of normal) behaviors are required to make a diagnosis of ASD
  - Age, developmental level, expressive language level, culture, and context (e.g., different settings or social circumstances) can significantly affect how behaviors manifest

ASD defies generalization

Measured Intelligence
Severely Impaired----------Gifted

Social Interaction
Aloof----------Passive----------Active but odd

Communication
Nonverbal----------Verbal

Behaviors
Intense----------Mild

Sensory
Sensory-seeking----------Sensory aversions

Motor
Uncoordinated----------Coordinated

Rising Rates

Identified Prevalence of Autism Spectrum Disorders
ADDM Network 2000-2008
Combining Data from All Sites

Surveillance Year	Birth Year	Number of ADDM Sites Reporting	Prevalence per 1,000 Children (Range)	This is about 1 in X children...
2000	1992	6	6.7 (4.5-9.9)	1 in 150
2002	1994	14	6.6 (3.3-10.6)	1 in 150
2004	1996	8	8.0 (4.6-9.8)	1 in 125
2006	1998	11	9.0 (4.2-12.1)	1 in 110
2008	2000	14	11.3 (4.8-21.2)	1 in 88

Rising ASD prevalence*

- Older studies focused primarily on more narrowly defined “autism”
  - More recent studies look at combined PDD
- Recent surveys suggest that rates can be as high has 1 in 50 (NCHS, 2013)

Changes in epidemiology: ASD and other conditions

- Historically, 70%-85% of autism cases were associated with intellectual disability, but this is no longer the case
  - 14 recent population-based studies reported IQ data: Across samples 30% to 85.3% had IQ in the average range
- 75%-90% of children with ASD acquire some functional language (compared to earlier estimate of 50%)

ASD is a developmental disorder

- Symptoms and behaviors change with development
- Development is affected by having ASD

Changes in epidemiology (cont.)

- Male to female ratio range = 2.7:1 to 15.7:1 (median 4.9:1)
- Regression rates initially estimated at 30% (Lotter, 1966)
  - Recent estimates range from 12.5% to 38.6% (median 23%)

Autism and Immunization

- Very difficult to identify a true regression
- 30 to 40% of parents report regression

- A smaller percentage of parents feel very passionately, that the onset of their child's autism is associated with some temporal event, like an illness, or a vaccination

Regression and Immunizations

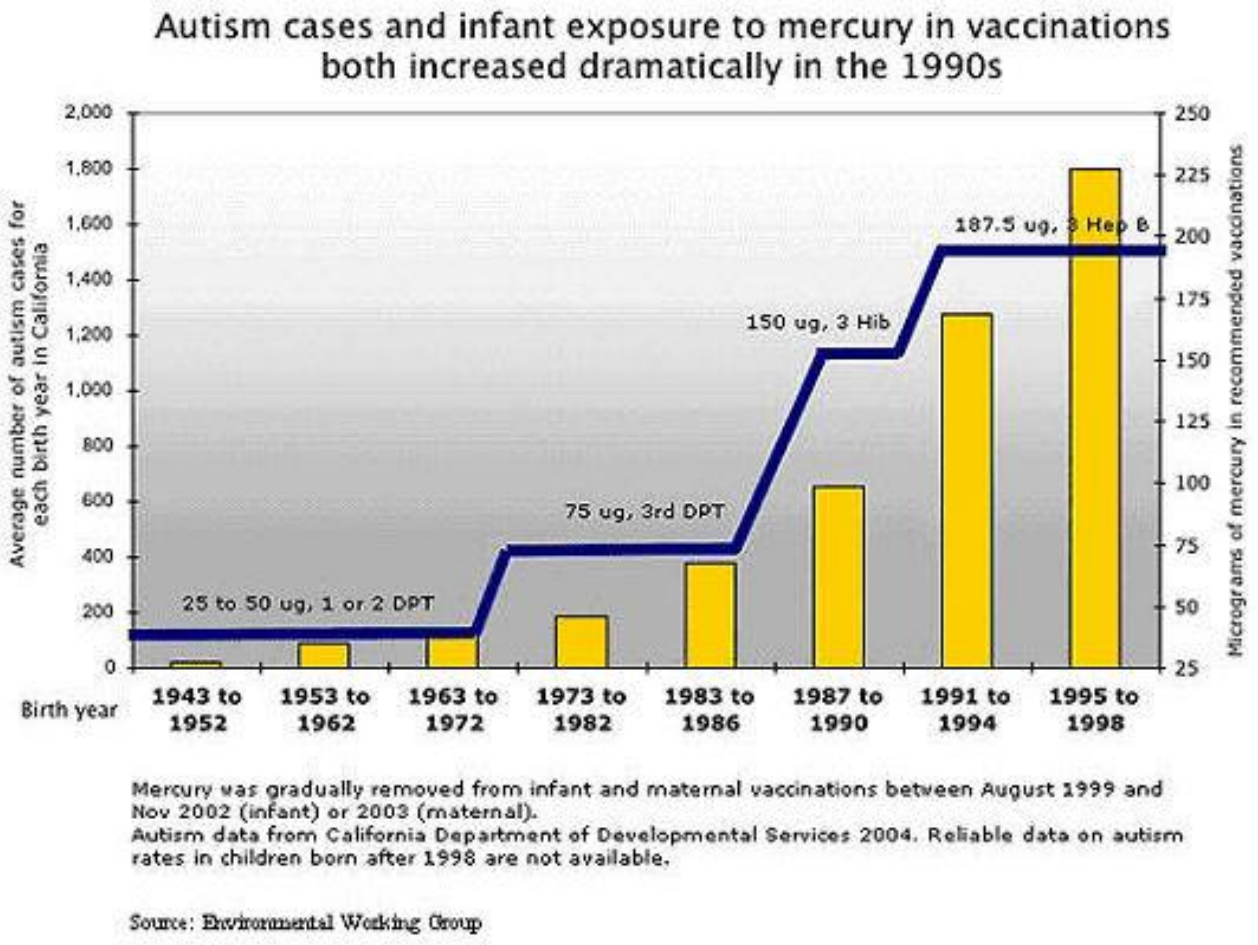
Journal of Autism and Developmental Disorders, Vol. 36, No. 3, April 2006 (© 2006)

Is There a 'Regressive Phenotype' of Autism Spectrum Disorder Associated with the Measles-Mumps-Rubella Vaccine? A CPEA Study

Jennifer Richler,[1] Rhiannon Luyster,[1] Susan Risi,[1] Wan-Ling Hsu,[1] Geraldine Dawson,[2] Raphael Bernier,[2] Michelle Dunn,[3] Susan Hepburn,[4] Susan L. Hyman,[5] William M. McMahon,[6] Julie Goudie-Nice,[6] Nancy Minshew,[7] Sally Rogers,[8] Marian Sigman,[9] M. Anne Spence,[10] Wendy A. Goldberg,[10] Helen Tager-Flusberg,[11] Fred R. Volkmar,[12] and Catherine Lord[13]

A multi-site study of 351 children with Autism Spectrum Disorders (ASD) and 31 typically developing children used caregiver interviews to describe the children's early acquisition and loss of social-communication milestones. For the majority of children with ASD who had experienced a regression, pre-loss development was clearly atypical. Children who had lost skills also showed slightly poorer outcomes in verbal IQ and social reciprocity, a later mean age of onset of autistic symptoms, and more gastrointestinal symptoms than children with ASD and no regression. There was no evidence that onset of autistic symptoms or of regression was related to measles-mumps-rubella vaccination. The implications of these findings for the existence of a 'regressive phenotype' of ASD are discussed.

Why the concern?



Why the Concern?

THE LANCET • Vol 351 • February 28, 1998

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology**

- n = 12 children with a chronic colitis and regressive *developmental disorder*
- found that 9 had autism, and after all the medical testing, they reported an association with the MMR vaccine, based on parent report

Autism and Immunizations

THE LANCET • Vol 353 • June 12, 1999

ARTICLES

Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association

Brent Taylor, Elizabeth Miller, C Paddy Farrington, Maria-Christina Petropoulos, Isabelle Favot-Mayaud, Jun Li, Pauline A Waight

- n = 498 cases of autism born in UK since 1979
- looked for a change in the amount of cases identified or a change in the age of onset that was associated with the introduction of the MMR vaccination in 1988

Interpretation Our analyses do not support a causal association between MMR vaccine and autism. If such an association occurs, it is so rare that it could not be identified in this large regional sample.

Autism and Immunizations

Danish Epidemiology Science Centre

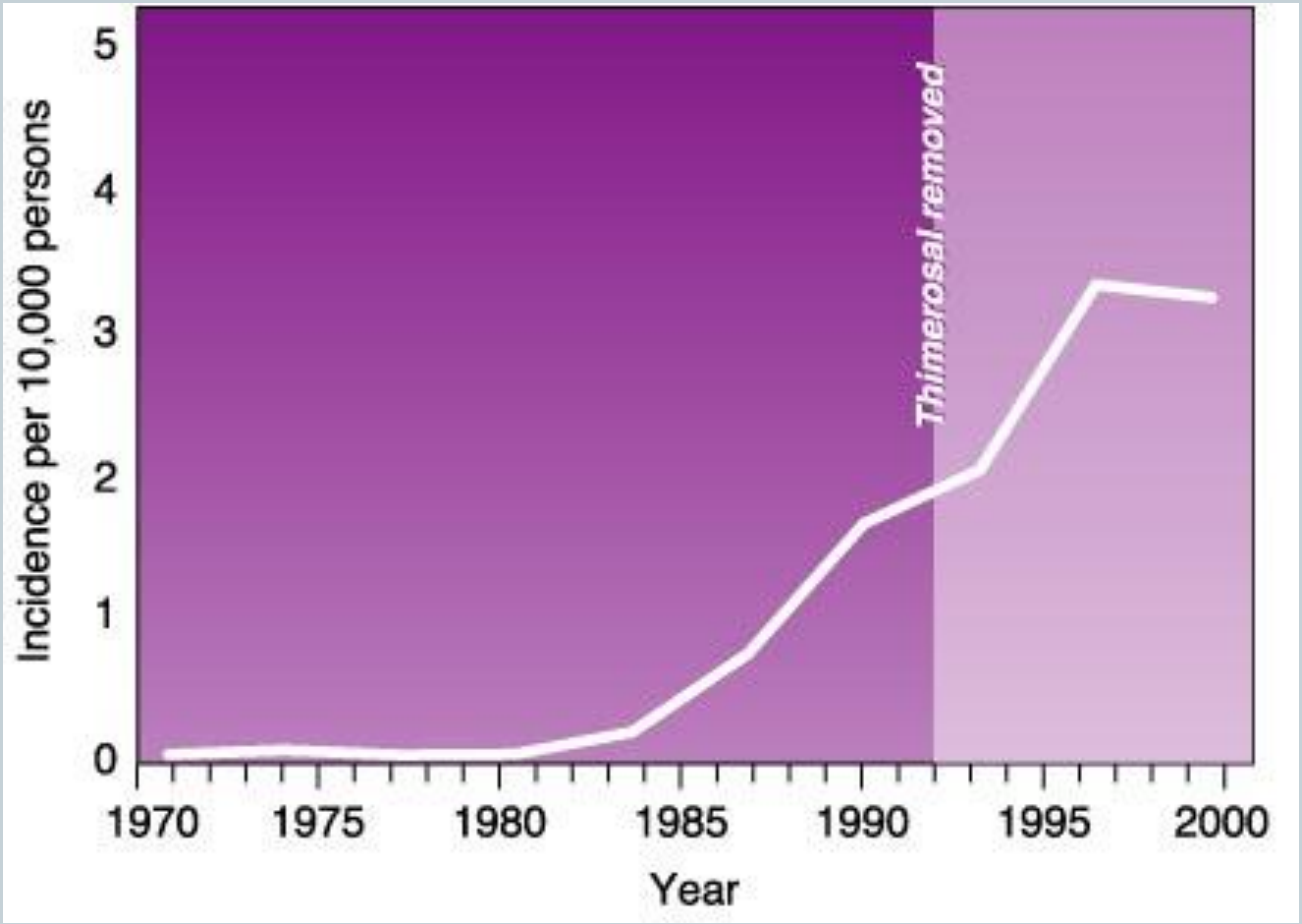
Association Between Thimerosal-Containing Vaccine and Autism

Anders Hviid, MSc; Michael Stellfeld, MD; Jan Wohlfahrt, MSc; Mads Melbye, MD, PhD

JAMA. 2003;290:1763-1766.

Results: We identified 1227 cases of autistic-spectrum disorders. The risk did not differ significantly between children vaccinated with thimerosal-containing vaccine and children vaccinated with thimerosal-free vaccine for autistic-spectrum disorders. Furthermore, we found no evidence of a dose-response association (ethylmercury) for autism and for other autistic-spectrum disorders.

No More Mercury



Autism and Immunizations

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Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta

Frank DeStefano, Tanya Karapurkar Bhasin, William W. Thompson, Marshalyn Yeargin-Allsopp and Coleen Boyle

Pediatrics 2004;113;259-266

From the *National Immunization Program, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia; ‡Battelle Memorial Institute, Cen-

Objective. To compare ages at first measles-mumps-rubella (MMR) vaccination between children with autism and children who did not have autism in the total population and in selected subgroups, including children with regression in development.

Autism and Immunizations

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Results. No significant associations for either of these age cutoffs were found for specific case subgroups, including those with evidence of developmental regression.

Autism and Immunizations

PEDIATRICS®
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Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links With Immunizations

Eric Fombonne, MD*, Rita Zakarian, MEd*, Andrew Bennett, PhD, CPsych*, Lingyan Meng, MSc*, Diana McLean-Heywood, MA*

OBJECTIVES. The purpose of this work was to estimate the pervasive developmental disorder prevalence in Montreal, Canada, in cohorts born from 1987 to 1998 and evaluate the relationship of trends in pervasive developmental disorder rates with: (1) changes in cumulative exposure to ethylmercury (thimerosal) occurring through modifications in the immunization schedule of young children and (2) trends in measles-mumps-rubella vaccination use rates and the introduction of a 2–measles-mumps-rubella dosing schedule during the study period.

Autism and Immunizations

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Eric Fombonne, MD*, Rita Zakarian, MEd*, Andrew Bennett, PhD, CPsych*, Liayan Meng, MSc*, Diana McLean-Heywood, MA*

METHODS. We surveyed 27 749 children born from 1987 to 1998 attending 55 schools from the largest Anglophone school board. Children with pervasive developmental disorders were identified by a special needs team. The cumulative exposure by age 2 years to thimerosal was calculated for 1987–1998 birth cohorts.

Autism and Immunizations

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RESULTS. We found 180 children (82.8% males) with a pervasive developmental disorder diagnosis who attended the surveyed schools, yielding a prevalence for pervasive developmental disorder of 64.9 per 10 000. The prevalence for specific

study period. The prevalence of pervasive developmental disorder in thimerosal-free birth cohorts was significantly higher than that in thimerosal-exposed cohorts (82.7 of 10 000 vs 59.5 of 10 000). Using logistic regression models of the preva-

2010: Too Little, Too Late?

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities, ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls ($p=0.003$), low haemoglobin in four children, and low serum IgA in four children.

Interpretation We identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

Lancet 1998; **351:** 637–41
See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology** (S H Murch MB, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP,), **Child and Adolescent Psychiatry** (M Berelowitz FRCPsych), **Neurology** (P Harvey FRCP), **and Radiology** (A Valentine FRCR), **Royal Free Hospital and School of Medicine, London NW3 2QG, UK**

Correspondence to: Dr A J Wakefield

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (diarrhoea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for a week, accompanied by their parents.

Clinical investigations

We took histories including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.[1] Developmental assessment included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.[2] Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

A New Angle on an Old Question?

THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Increasing Exposure to Antibody-Stimulating Proteins and Polysaccharides in Vaccines Is Not Associated with Risk of Autism

Frank DeStefano, MD, MPH[1], Cristofer S. Price, ScM[2], and Eric S. Weintraub, MPH[1]

Objective To evaluate the association between autism and the level of immunologic stimulation received from vaccines administered during the first 2 years of life.

Study design We analyzed data from a case-control study conducted in 3 managed care organizations (MCOs) of 256 children with autism spectrum disorder (ASD) and 752 control children matched on birth year, sex, and MCO. In addition to the broader category of ASD, we also evaluated autistic disorder and ASD with regression. ASD diagnoses were validated through standardized in-person evaluations. Exposure to total antibody-stimulating proteins and polysaccharides from vaccines was determined by summing the antigen content of each vaccine received, as obtained from immunization registries and medical records. Potential confounding factors were ascertained from parent interviews and medical charts. Conditional logistic regression was used to assess associations between ASD outcomes and exposure to antigens in selected time periods.

Results The aOR (95% CI) of ASD associated with each 25-unit increase in total antigen exposure was 0.999 (0.994-1.003) for cumulative exposure to age 3 months, 0.999 (0.997-1.001) for cumulative exposure to age 7 months, and 0.999 (0.998-1.001) for cumulative exposure to age 2 years. Similarly, no increased risk was found for autistic disorder or ASD with regression.

Conclusion In this study of MCO members, increasing exposure to antibody-stimulating proteins and polysaccharides in vaccines during the first 2 years of life was not related to the risk of developing an ASD. *(J Pediatr 2013;■:■-■).*

New Angel, Old Question: Japan

The combined measles, mumps, and rubella vaccines and the total number of vaccines are not associated with development of autism spectrum disorder: The first case–control study in Asia

Yota Uno[a,b,*], Tokio Uchiyama[b,c], Michiko Kurosawa[d], Branko Aleksic[a], Norio Ozaki[a]

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[b] Yokohama Psycho-Developmental Clinic, Yokohama, Japan
[c] Department of Faculty of Human Development, Fukushima University Graduate school, Fukushima, Japan
[d] Department of Epidemiology and Environmental Health, Juntendo University Graduate School of Medicine, Tokyo, Japan

A B S T R A C T

Objective: The aim of this study was to investigate the relationship between autism spectrum disorder (ASD) and general vaccinations, including measles–mumps–rubella (MMR) vaccine, in Japanese subjects, a population with high genetic homogeneity.

Patients and methods: A case–control study was performed. Cases ($n = 189$) were diagnosed with ASD, while controls ($n = 224$) were volunteers from general schools, matched by sex and birth year to cases. Vaccination history and prenatal, perinatal, and neonatal factors from the Maternal and Child Health handbook, which was part of each subject's file, were examined. To determine the relationship between potential risk factors and ASD, crude odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated, and the differences in mean values of the quantitative variables between cases and controls were analyzed using an unpaired *t*-test. Moreover, MMR vaccination and the effect of the number of vaccine injections were investigated using a conditional multiple regression model.

Results: For MMR vaccination, the OR was 1.04 (95% CI, 0.65–1.68), and no significant differences were found for the other vaccines. For all of the prenatal, perinatal and neonatal factors, there were no significant differences between cases and controls. Furthermore, regarding the presence of ASD, MMR vaccination and the number of vaccine injections had ORs of 1.10 (95% CI, 0.64–1.90) and 1.10 (95% CI, 0.95–1.26), respectively, in the conditional multiple regression model; no significant differences were found.

Conclusions: In this study, there were not any convincing evidences that MMR vaccination and increasing the number of vaccine injections were associated with an increased risk of ASD in a genetically homogeneous population. Therefore, these findings indicate that there is no basis for avoiding vaccination out of concern for ASD.

Why?

- The mystery of autism?
  - What is it?
  - What causes it?
  - Why the rise in rates?
- Most don't understand
  - Leaves the door open
  - People look for an obvious answer
- We need to educate better!

What is Autism?

Impaired Learning and Perception

Pervasive Developmental Delays

AUTISM

What to Do About It?

- Earlier Detection
  - Get to a place where we can detect autism before MOST vaccines!
  - Move away from waiting for behaviors to emerge.
  - Understand the infant brain.

Until Then: NODA

Apr 16, 2013 | 10:28 PM Shopping | Jobs | Cars | Real Estate | Rentals | Bu

azcentral.com

App would give parents a faster autism diagnosis

It would allow kids to get earlier, more-effective treatment

Dr. Chris Smith works with Blake Allen, 2, at the Southwest Autism Research and Resource Center.

Pat Shannahan/The Republic

USA TODAY NEWS SPORTS

This story is part of
HEALTH AND WELLNESS

App aims fo

Until Then: SARRC

- *Advance research and provide support to individuals with ASD and their families.*
  - *Early education for newly diagnosed families*
  - *Early intervention: Inclusive preschool, in home parent training*
  - *School consulting*
  - *'Tween programs*
  - *Social skills training and psychological counseling*
  - *Teen Programs: Community Works*
  - *Adult Programs: Life Skills and employment!*
  - *Research Programs: Clinical Trials and improved detection*
- *Let's focus less on the cause and more on the people!*

Thank you for your attention!

Questions?

SARRC

www.autismcenter.org

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